REMARKS

Claims 1 and 5 have been amended. Claims 3 and 6 have been canceled. Claims 7-11 have been withdrawn from consideration as being directed to non-elected inventions. Thus, claims 1, 2, 4, 5 and 7-11 are pending in the present application, with claims 1, 2, 4 and 5 currently under consideration. Support for the amendment to claim 1 may be found in original claim 3. Thus, no new matter has been added. Reconsideration and withdrawal of the present rejections in view of the remarks presented herein are respectively requested.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-6 were rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. The Examiner contends that although the claimed method is enabling with regard to a compound of formula I, in which the substituents are those of the elected species (PPK-5), the specification does not reasonably provide enablement for any and all such T-type calcium channel blockers that exhibit the same activity. Claim 1 as amended no longer recites all selective T-channel antagonists, but limits the claim to those antagonists encompassed by formula I. Applicants note that the Examiner has acknowledged that the elected species is enabled by the specification. However, the Examiner has provided no evidence as to why the specification does not provide enablement for other compounds falling within the scope of formula I as recited in amended claim 1 (i.e., why other compounds encompassed by claim 1 would not have the onset and duration of activity in reducing systolic blood pressure). With regard to the enablement requirement, M.P.E.P. § 2164.04 states that:

> In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370

> (CCPA 1971). As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." 439 F.2d at 224, 169 USPQ at 370.

In the Office Action at page 4, the Examiner contends that "*this variable list of Markush members would result in undue experimentation because having to determine the activity of each and every T-type agonist would be burdensome. The amount of direction and guidance in order to clearly determine each and every T-type channel antagonist would meet each and every limitation of claim 1 is absent in the specification.*" However, the Examiner has provided no credible scientific reasoning or evidence as to why other compounds falling within the scope of claim 1 are not enabled by the present specification. The present specification clearly describes numerous compounds falling within the scope of formula I (see pages 13-16, paragraph [0058] and page 17, Table 1). In addition, the specification at page 69, Example 50, describes an *in vivo* protocol for a blood pressure study in spontaneously hypertensive rats (SHR). Results obtained for the elected species, PPK-5, using this type of protocol, are described at page 30, paragraphs [0101] and [0102]. This protocol could be used to test the ability of any compound falling within the scope of claim 1 to have the recited activity in reducing systolic blood pressure. Thus, the specification provides sufficient guidance to one of ordinary skill in the art for selecting compounds falling within the scope of claim 1 that have the activity recited in claim 1. Although the experimentation may be tedious, it is certainly not undue. According to M.P.E.P. §2164.01:

> The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm"n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

One of ordinary skill in the art of researching pharmaceuticals for treating hypertension could routinely perform the types of animal studies described in the present specification to determine the *in vivo* activity and PK characteristics of potential antihypertensive agents. The

standard is not the level of experimentation required to test *every conceivable* compound; rather, it is the amount of experimentation required to screen a particular candidate. In light of the foregoing, this modest amount of experimentation cannot be considered undue.

This is consistent with *In re Wands*, cited by the PTO. In that case, the question was whether undue experimentation was required to generate monoclonal antibodies against Hepatitis B. The Federal Circuit looked only to the amount of experimentation required to generate ONE such antibody, not the huge number of theoretically-possible antibodies.

In view of the comments presented above, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. 102(b)

Claims 1-6 were rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Kumar et al. (*Molecular Pharmacology 61*:649-658, 2002). Claim 1 recites that a selective T-channel antagonist is provided which has an onset of activity in reducing systolic blood pressure *in vivo* of at least three hours and a duration of activity *in vivo* of at least 24 hours, and that the compound is administered in regular doses no more often than once per day. The Examiner contends that the recited activities of the claimed T-channel antagonists are inherently disclosed by Kumar et al. and cites Figures 6A-B of Kumar in support of this contention. In addition, the Office Action alleges that the recitation of "in regular doses no more often than once per day" would be inherently present in the cited reference. This latter statement is clearly incorrect.

According to M.P.E.P. § 2112 IV, to support a rejection based on inherency, the Examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the characteristic alleged to be inherent by the Examiner **necessarily** flows from the teachings of the applied prior art. *Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)*. (emphasis added) "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." (emphasis added) *In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)*. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is **necessarily present** in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established

by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999).* (Emphasis added).

Every compound has an inherent set of properties. Applicants acknowledge that the Kumar et al. compounds inherently have onset and duration of activity properties. That is not the inherency that is at issue here. Instead, the issue is whether the recited dosing is **necessarily present** in the reference. It is not.

By analogy, the antibiotic cyclosporine was not initially known to have inherent immune-suppression properties. At that time, a person administering the drug to patients would not have been able to take advantage of that property. Thus, they would not **necessarily** have given the drug to organ transplant patients to fight rejection of the new organ, and an inherency rejection based on such dosing would not be proper.

In a similar way, because the art was silent about the pharmacokinetic properties of the compounds tested by Kumar et al, no dosing schedule is inferred. Thus, no one would have **necessarily** dosed this drug by "administering the antagonist to a mammal in regular doses no more often than once per day . . .." The Kumar et al. reference, including Figures 6A-B, are silent about the onset of activity/duration of those compounds. If one is unaware of an inherent property, one would not adjust the use of a compound to take advantage of that unappreciated property.

Because the claimed dosing schedule is not in the prior art, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b).

CONCLUSION

No fees are believed to be due. However, please charge any fees, including any fees for extensions of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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By: _____

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